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Effects of Obesity in Pregnancy

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Introduction

Obesity is a major health problem that affects many people. The current professional recommendations for weight gain in pregnancy among overweight and obese women are both vague and variable, in that they are generalized to the population rather than catered to individual risk factors. Women who exhibit excessive weight gain and obesity prior to and throughout pregnancy are more likely to experience worsening metabolic and cardiac complications, higher rates of maternal morbidity and mortality, as well as poorer neonatal and fetal outcomes. Women who have preexisting cardiac or metabolic conditions have exacerbated symptoms throughout pregnancy due to the increased cardiac and metabolic demands. In addition, many develop secondary cardiac and metabolic complications into the immediate postpartum period that persist beyond that as well. It is important to discuss the problems that women face in regards to obesity during pregnancy because of the lack of emphasis on risk reduction strategies to prevent and minimize cardiac and metabolic manifestations and ramifications that arise as a result. Although a significant amount of research has been conducted that proves the negative effects of obesity and excessive weight gain on pregnancy, effective management and treatment has done very little to remedy the root of the problem; the lack of focus in developing preventative strategies to reduce risk factors that perpetuate high maternal and fetal morbidity and mortality.

The main focus of this thesis is a comprehensive review of the literature pertaining to the issue of excessive weight gain and obesity within the context of pregnancy. It will consist of a description of the extent to which excessive weight gain and obesity is significant to the degree of risk and likelihood of pregnancy complications, a description of the current weight gain recommendations in pregnancy, and an outline of the normal cardiac and metabolic changes and demands that occur as a result of pregnancy. Furthermore, an understanding of the most

common conditions associated with obesity and excessive weight gain during pregnancy will be discussed in terms of definition, pathophysiology, symptomology and patient outcomes, and treatment. In addition, the neonatal and fetal complications as well as the long-term maternal consequences that arise secondary to maternal obesity and excessive weight gain throughout pregnancy will be explored.

Excessive weight gain and obesity prior to and throughout pregnancy is a serious risk factor that greatly contributes the development of gestational hypertension and preeclampsia, gestational diabetes mellitus, cardiovascular disease and peripartum cardiomyopathy, as well as and numerous adverse neonatal and fetal outcomes. In this respect, preventions and future strategies must be focused on conducting more research and implementing more teaching to promote healthy lifestyle choices, including weight loss, maintenance, and control, prior to, throughout, and following pregnancy, in order to improve maternal cardiovascular and metabolic health, decrease maternal mortality rates, as well as increase positive pregnancy outcomes.

Significance of the Problem

Obesity and excessive weight gain throughout pregnancy is a problem of great significance. According to the American College of Obstetricians and Gynecologists (ACOG, 2013, No. 549), "in the United States, more than one third of women are obese, more than one half of pregnant women are overweight or obese, and 8% of reproductive-aged women are extremely obese, putting them at a greater risk of pregnancy complications." Obesity is defined and categorized by the calculation of body mass index (BMI), which is a ratio of a person's weight to height. "A person with a BMI less than 18.5 is considered to be underweight, from 18.5 to 24.9 is normal weight, from 25.0 to 29.9 is overweight, and greater than 30.0 is obese" (Morin & Reilly, 2007, p. 483). A good portion of women receive very little education or

counseling regarding how the safety and risks of pregnancy are affected by their weight status, since current recommendations are vague and often variable based on individualized risk factors and stressors. It has been found that "women with low pre-pregnancy BMI tend to underestimate their recommended weight gain for pregnancy, while obese women overestimated their recommended weight gain goals" (Smith, Husley, & Goodnight, 2008, p. 180). This suggests that better preventative strategies against obesity, goals for management of pre-pregnancy weight, and improved education regarding the recommended BMI-based weight gain during pregnancy be explored and reiterated. These strategies, goals, and teaching tactics about weight management throughout pregnancy and prevention of obesity-related problems (such as weight retention) in the postpartum period should be implemented prior to, during, and after pregnancy to reduce the risk and likelihood of adverse maternal and fetal complications in pregnancy.

Specifically, through the review of the current literature, it is understood that excessive weight gain and obesity during pregnancy increases the risk for developing maternal complications, such as gestational hypertension, preeclampsia, gestational diabetes mellitus, and heart failure (i.e., peripartum cardiomyopathy). Furthermore, excessive weight gain and obesity contributes to poor neonatal and fetal outcomes in relation to labor & delivery as well as growth & development. These include fetal macrosomia and large for gestational age (high birth weight), small for gestational age (low birth weight), increased incidence of prematurity and/or stillbirth, increased likelihood of cesarean birth with possible birth injury, and a variety of birth defects and congenital anomalies. The fact that excessive weight gain and obesity greatly contributes to adverse maternal and fetal outcomes is supported by statistics. "Excessive maternal weight gain during pregnancy was associated with a doubling of the risk of large for gestational age neonates. Overall, maternal obesity is associated with a doubling of risk for

hypertensive disorders of pregnancy, cesarean delivery, and macrosomia, as well as a nearly fourfold increase in gestational diabetes" (Smith, et. al, 2008, p. 179). "Morbidly obese women are almost five times more likely to develop preeclampsia, even when diabetes and hypertension are taken into account" (Morin & Reilly, 2007, p. 483). In other words, excessive weight gain and obesity directly affects the likelihood of developing preeclampsia in pregnancy, regardless of preexisting diabetes or high blood pressure. In addition, cardiac complications can arise throughout pregnancy secondary to excessive weight gain and obesity. "Heart disease complicates more than 1% of pregnancies and is now the leading cause of indirect maternal deaths" (Simpson, 2012, p. 345). In particular, excessive weight gain and obesity exacerbates underlying heart conditions due to the increased cardiac demands throughout pregnancy. Hemodynamic changes in pregnancy include "expected increases in preload, cardiac output, and oxygen consumption coupled with the normal decrease in afterload", which "may unmask or worsen cardiac disease in the pregnant woman" (Simpson, 2012, p. 347). In addition, "in women without recognized heart disease, the diagnosis is often delayed because complaints of shortness of breath, decreased exercise tolerance, and peripheral edema are attributed to normal pregnancy" (Simpson, 2012, p. 347). It also elevates the risk for developing cardiac problems, even without previous cardiac history. This is the case when it comes to peripartum cardiomyopathy, which is defined as heart failure and left ventricular dysfunction that occurs in the last month of pregnancy or within five months postpartum, in which no other cause can be attributed for symptoms of heart failure. Overall, pre-pregnancy obesity is a known risk factor for the development of peripartum cardiomyopathy, and excessive weight gain and retention contribute to the increased cardiac workload and the worsening of cardiac symptoms and conditions throughout and following pregnancy.

After pregnancy runs its course and women who are obese or were overweight throughout their pregnancy have entered the immediate postpartum period, there is an increased risk for postpartum weight retention and subsequent problems with chronic obesity, especially if there is a failure to return to pre-pregnancy weight. It was discovered that "women who gain more weight than recommended retain twice as much weight after pregnancy as women who gain within the recommendations" (Walters & Taylor, 2009-2010, p. 491). "Persistence of maternal pregnancy weight gain may lead to an increase in BMI during subsequent pregnancies. Women who increase their weight considerably during their first pregnancy or retained weight after delivery have the highest risk for subsequent weight gain in future pregnancies"(Smith et. al, 2008, p. 179-180). "High gestational weight gain appears to be associated with both short and long-term pregnancy weight retention. Overweight women who over-gain during pregnancy are at increased risk for becoming obese postpartum" (Langford, Joshu, Chang, Myles & Lett, 2011, p. 861). These facts lead to the conclusion that medical counseling regarding weight reduction prior to pregnancy and/or an adherence to weight gain only within IOM and ACOG recommendations among obese women are essential to improve pregnancy outcomes.

Weight Gain Recommendations during Pregnancy

There are specific weight gain guidelines during pregnancy of which overweight and obese women are recommended to adhere to in order to reduce risk for maternal and fetal complications and improve pregnancy outcomes. "The 2009 IOM guidelines recommend a total weight gain of 15-25 lb (6.8-11.3 kg) for overweight women (BMI = 25-29.9) and 11-20 lb (5.0-9.1 kg) for all obese women (BMI $\geq$ 30). These ranges are independent of age, parity, smoking history, race, and ethnic background" (ACOG, 2013, No. 549). Most recently, IOM recommendations expanded in scope to include suggested weight gain intervals among

overweight and obese women who were expecting multiparous pregnancies. "For twin pregnancy, the IOM recommends a gestational weight gain of 16.8-24.5 kg (37-54 lb) for women of normal weight, 14.1-22.7 kg (31-50 lb) for overweight women, and 11.3-19.1 kg (25-42 lb) for obese women. The IOM guidelines recognize that data are insufficient to determine the amount of weight women with multifetal (triplet and higher order) gestations should gain" (ACOG, 2013, No. 548).

The updated IOM recommendations have been met with controversial reactions due to the belief that weight gain targets are too high, especially for overweight and obese women and do not address concerns regarding postpartum weight retention. Although the IOM defines obesity, it is a very broad and all-encompassing definition, in that they do not differentiate between classes of obesity (i.e., Class 1 is a BMI of 30-34.9; Class 2 is a BMI of 35-39.9; and Class 3 is a BMI of 40 or greater). "Citing a lack of sufficient data regarding short-term and long-term maternal and newborn outcomes, authors of the IOM report did not recommend lower targets for women with more severe degrees of obesity, (and) the results of observational studies continue to provide mixed results" (ACOG, 2013, No. 548). It has been consistently found that "gestational weight gain below the IOM recommendations among overweight pregnant women does not appear to have a negative effect on fetal growth or neonatal outcomes. For the overweight pregnant women who is gaining less than the recommended amount but has an appropriately growing fetus, no evidence exists that encouraging increased weight gain to conform with the current IOM guidelines will improve maternal or fetal outcomes" (ACOG, 2013, No. 548). In other words, many studies have suggested that overweight women who gained less weight than is recommended (i.e., only 2.7-6.4 kg, or 6-14 lb) had similar fetal

growth, perinatal and neonatal outcomes, and less postpartum weight retention as overweight women who gained weight within the currently recommended IOM range.

In light of these specific guidelines for maternal weight gain among overweight and obese women, there are only general recommendations for obese women who are pregnant or planning a pregnancy in regards to risk reduction strategies in preventing obesity-related maternal and fetal/neonatal complications and adverse outcomes. ACOG purports that "preconception assessment and counseling are strongly encouraged and should include the provision of specific information concerning the maternal and fetal risks of obesity in pregnancy. At the initial prenatal visit, height and weight should be recorded for all women to allow calculation of BMI, and recommendations for appropriate weight gain, guided by IOM recommendations, should be reviewed both at the initial visit and periodically throughout pregnancy. Nutrition consultation should be offered to all overweight or obese women, and they should be encouraged to follow an exercise program. Nutrition and exercise counseling should continue postpartum and before attempting another pregnancy" (ACOG, 2013, No. 549). It is evident that these recommendations are extremely vague and do very little as far as planning for a pregnancy complicated by obesity or in maintaining appropriate weight gain in pregnancy.

It is obvious that more observational and quantitative research must be conducted about the effects of different classes of obesity (Class 1, 2, & 3) on the short and long-term maternal and neonatal/fetal risks/outcomes of pregnancy. The results that come from these prospective studies will hopefully serve to be more valid and consistent in nature. At this time, the review of the literature from previous studies is limited and the results are contradictory and show significant variation. The effects of excessive weight gain and obesity on maternal outcomes, the development of peripartum complications (i.e., gestational hypertension, preeclampsia,

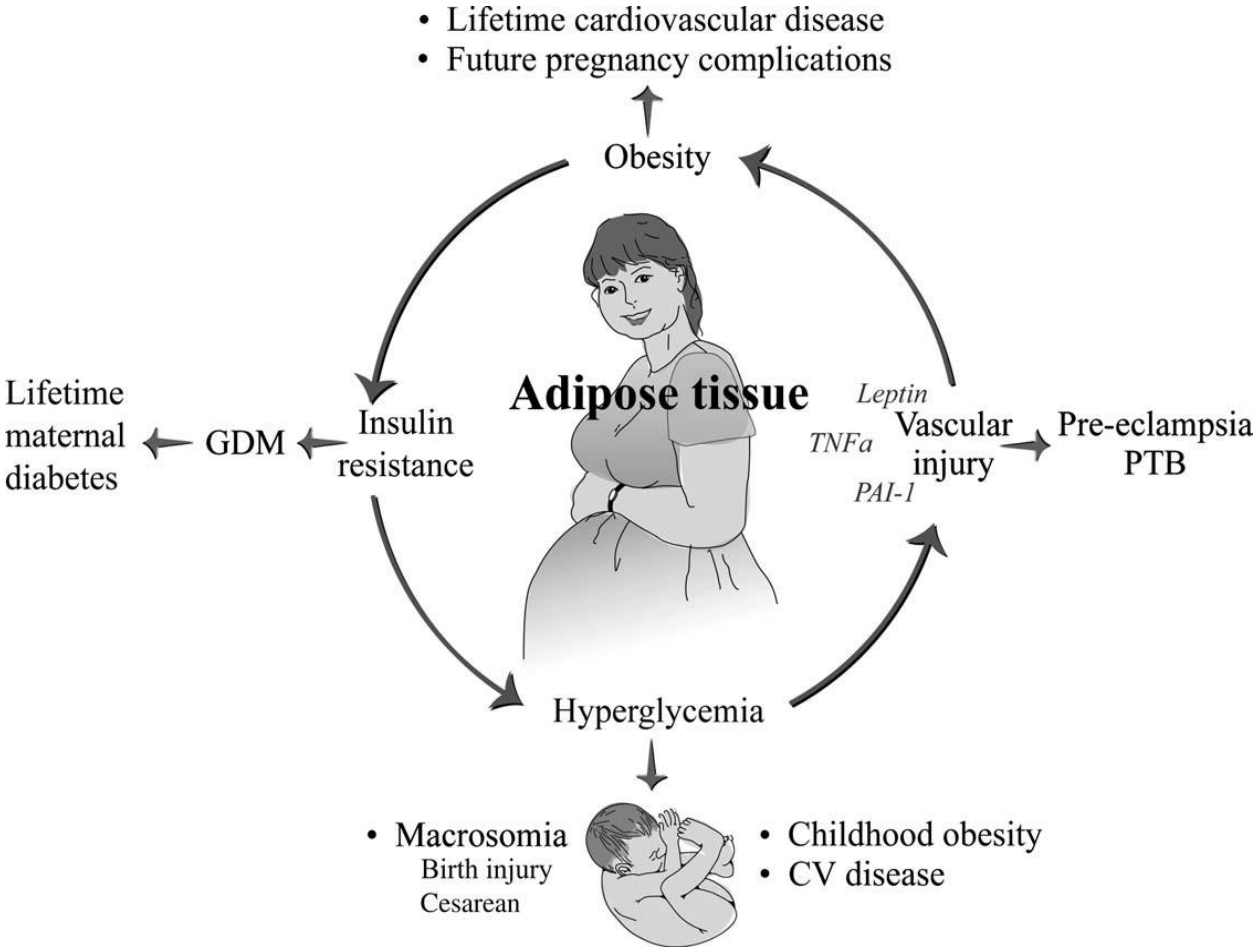
gestational diabetes mellitus, and cardiomyopathy/heart failure), and the likelihood/risk of postpartum weight retention are much more universal and simplistic, yet "the gestational weight gain guidelines attempt to balance the risks of having large-for-gestational age infants, small-for-gestational age infants, and preterm births and postpartum weight retention" (ACOG, 2013, No. 548). Therefore, the effects of pre-pregnancy BMI (i.e., overweight, obese) and gestational weight gain on fetal outcomes and the development of fetal complications during growth and development or in the process of labor and delivery (i.e., neural tube defects, macrosomia, prematurity, and stillbirth) are much more mixed and complicated. This is due to a lack of cohesiveness or agreement upon the validity and effectiveness of guidelines for weight gain among overweight and obese women during pregnancy. Until future research can provide evidence-based practice that would further refine the recommendations for gestational weight gain among women with higher degrees of obesity, the fact will remain that "the relationships between maternal obesity class, gestational weight gain, and maternal and newborn outcomes are complex" (ACOG, 2013, No. 548). Overall, the major outcomes of pre-pregnancy obesity and gestational weight gain have maternal and fetal/neonatal implications that affect pregnancy-related morbidity and mortality.

Normal Physiological Changes and Demands of Pregnancy

The normal physiological changes and demands of pregnancy mainly affect the cardiovascular and endocrine systems of the body. In general, there is an overall increase in blood volume and a greater degree of oxygen consumption, which is accounted for by variability in blood pressure and elevated heart rate. Therefore, there is an increase in cardiac workload and strain because the heart as a pump cannot contract as effectively in order to compensate for such a large change in blood volume. Maternal metabolism is drastically altered due to rising levels

of circulating hormones (specifically, estrogen and progesterone) that contribute to increased maternal insulin resistance coupled with decreased sensitivity of body cells to the effects of insulin, which relates to the pathological elevation in blood glucose levels throughout pregnancy. Prolonged hyperglycemia begins to affect the integrity of both preexisting and newly formed blood vessels, leading to vascular injury and dysfunction related to vasoconstriction and chronic inflammation within the vasculature. The vasconstrictive and inflammatory damage inflicted on the blood vessels result in subsequent elevations in blood pressure. Large concentrations of circulating glucose along with long intervals of vasoconstriction and hypertension contribute to an increased risk for developing gestational diabetes mellitus and preeclampsia (gestational hypertension), respectively. Prolonged hyperglycemia and insulin resistance coupled with a diagnosis of GDM significantly elevates the likelihood for the occurrence of fetal macrosomia (large-for-gestational age infants) and birth injuries, defects, and/or higher rates of cesarean deliveries. On the other hand, prolonged vasoconstriction and gestational hypertension with a concurrent diagnosis of preeclampsia result in a higher risk for fetal prematurity as well as other associated conditions such as intrauterine growth restriction (IUGR) and low birthweight infants (Davidson, London & Ladwig, 2012).

The Pathophysiology of Obesity in Pregnancy



Smith, S.A., Husley, T. & Goodnight, W., Effects of obesity on pregnancy. *Journal of Obstetric, Gynecological, and Neonatal Nursing*, 37(2), 2008, p. 178

The pathophysiology of obesity when combined with the normal pathological effects that occur during pregnancy further compound the risks and issues surrounding the development of adverse maternal and fetal outcomes. Obesity and excessive weight gain are associated with a greater amount of adipose (fatty) tissue that has been deposited in the body, including within the placenta. Leptin, also known as the "obesity hormone", is a protein released by adipose tissue that regulates fat metabolism and storage in addition to controlling the mechanisms of appetite. The level of circulating leptin is directly proportional to the amount of fatty tissue that is stored in the body. Overweight and obese individuals experience higher levels of circulating leptin,

leading to the desensitization and resistance from body cells to the effects of leptin. This allows for increased build-up of adipose tissue and uncontrolled increases in appetite, further perpetuating the cycle of obesity. "Obesity represents a state of altered hormonal and inflammatory activity, associated with the function of adipose or fatty tissue. Adipose tissue has been demonstrated to be a source of production of peptides and non-peptide compounds involved in cardiovascular homeostasis. The peptide, interleukin 6 (IL6) is secreted by adipose tissue and modulates the production of C-reactive protein (CRP). Elevated CRP is a known marker of a chronic inflammation associated with an increased risk of cardiovascular disease" (Smith, et. al., 2008, p. 177).

Excessive weight gain and obesity contributes to the exacerbation of the normal physiological changes that occur throughout pregnancy, especially when taking into account the alterations in cardiovascular and metabolic demands. "The typical increase in cardiac output associated with pregnancy is compounded when a woman is obese and is influenced by the degree and duration of obesity. Cardiac output increases by 30 to 50 ml/minute for every 100 g of fat deposited. Blood volume is increased as well. A degree of cardiac hypertrophy is normal during pregnancy, but obesity exaggerates the hypertrophy and contributes to myocardial dilation. Moreover, fat deposits in myocardial tissue contribute to conduction and contractility problems" (Morin & Reilly, 2007, p. 483). "Insulin resistance increases 50% to 60% over the course of a normal pregnancy, and obesity prior to and during pregnancy is strongly associated with impaired insulin sensitivity. Compared to women with normal glucose tolerance, obese women with gestational diabetes demonstrate even greater impairment in insulin resistance" (Smith, et. al., 2008, p. 177). "Obesity has also been associated with abnormal endothelial function, likely resulting in decreased nitric oxide (NO). The net result of a decrease in NO is an

increase in vascular resistance that may also increase the risk of cardiovascular disease. The result of this pro-inflammatory state, possibly mediated via increased insulin resistance is an obesity related increase in hypertension" (Smith, et. al., 2008, p. 178). "Obesity in pregnancy is associated with hyperinsulinemia and dyslipidemia, as well as altered endothelial function and a chronic inflammatory state. During pregnancy, this pro-inflammatory state is associated with an increased risk of preeclampsia and preterm birth." (Smith, et. al., 2008, p.178). All in all, as the figure above clearly illustrates, the cycle of obesity and excessive adipose tissue contributes to hyperglycemia, insulin resistance, and vascular injury, which gradually lead to the development of fetal macrosomia (LGA), birth injury/defect, cesarean delivery, and gestational diabetes mellitus (GDM), in addition to contributing to the pathophysiology of preeclampsia, preterm birth (IUGR, SGA, low birthweight) and cardiovascular disease.

Major Outcomes of Obesity in Pregnancy

1. *Maternal Complications*

A. Gestational Hypertension and Preeclampsia

Definition

Hypertension in pregnancy can be classified into four different categories "preeclampsia-eclampsia", "chronic hypertension", "chronic hypertension with superimposed preeclampsia", and "gestational hypertension". Chronic hypertension is often a precursor to preeclampsia, in that "preeclampsia develops in approximately 22% of women previously found to have chronic hypertension" (Davidson, et. al., 2012, p.476), yet preeclampsia can still be present during pregnancy without any signs of hypertension prior to pregnancy. In turn, chronic hypertension is associated with the vascular and pro-inflammatory changes that occur with obesity and is compounded by the normal physiological changes of the cardiovascular system throughout

pregnancy. "After 20 weeks' gestation the onset of proteinuria and worsening hypertension is suggestive of superimposed preeclampsia" (Davidson, et. al., 2012, p. 476). Gestational hypertension is a very common development in obese and overweight women, and the risk increases when these women have excessive weight gain throughout their pregnancies. It is defined as a prolonged yet transient elevation in blood pressure that is induced for the first time in the middle of the pregnancy, yet the woman exhibits no proteinuria or other signs of preeclampsia. "If preeclampsia does not develop and blood pressure returns to normal by 12 weeks' postpartum, the diagnosis of gestational hypertension may be assigned. If the blood pressure elevation persists after 12 weeks' postpartum, the woman is diagnosed with chronic hypertension" (Davidson, et. al. 2012, p. 476). "Chronic hypertension exists when the blood pressure is 140/90 or higher before pregnancy or before the 20th week of gestation or persists 42 days following childbirth" (Davidson, et. al., 2012, p. 475). "Preeclampsia, in particular, is a maternal pregnancy complication associated with high pre-pregnancy BMI and medically-induced preterm birth" (Madan, Chen, Goodman, Davis, Allan & Dammann, 2010, p. 82). In other words, for women who have chronic hypertension, regardless of whether they develop superimposed preeclampsia, will have increased risk of fetal growth restriction, preterm birth, and cesarean birth. "Preeclampsia was defined as pregnancy induced hypertension after the 20th week of gestation that resulted in an increase in blood pressure of $\geq$ 30 mm Hg systolic or $\geq$ 15 mm Hg diastolic on two measurements taken 6 h apart" (Langford, et. al., 2011, p. 861). There are numerous physiological mechanisms that contribute to the development of these various categories and combinations of hypertensive states during pregnancy.

Pathophysiology

The pathophysiology of the numerous hypertensive states in pregnancy, namely preeclampsia, is complex and not entirely known or understood. It is believed that there is impaired placental and endothelial function due to an imbalanced process of angiogenesis (the formation and vascularization of blood vessels), resulting in an exaggerated systemic inflammatory response of the placental vasculature. "In pregnancy, the pro-inflammatory state associated with obesity has been implicated in the pathophysiology of preeclampsia" (Madan et. al; 2010, p. 83). In addition, there is an imbalanced ratio between the prostaglandins prostacyclin (a vasodilator to decrease blood pressure, prevent platelet aggregation, and improve uterine blood flow) and thromboxane (a vasoconstrictor that promotes platelet aggregation), in that prostacyclin levels are diminished, allowing the effects of thromboxane to dominate (increasing blood pressure and decreasing uteroplacental blood flow, possibly resulting in ischemia). Furthermore, there is decreased production of nitric oxide (NO) within the placenta, which acts as a potent vasodilator to regulate maternal blood pressure. In this way, there is an overall increase in blood pressure within the uteroplacental vasculature as a result of overpowering vasoconstrictive mechanisms, leading to decreased placental perfusion and adverse neonatal outcomes (i.e., IUGR, chronic hypoxia, birth defects). "Because the inflammatory changes of normal pregnancy are exaggerated in hypertensive pregnancies, maternal factors that may exacerbate this inflammatory response, such as obesity, insulin resistance, and lipid abnormalities, predispose patients to endothelial dysfunction, preeclampsia, and potentially CVD in later life" (Bilhartz, T.D., Bilhartz, P.A., Bilhartz, T.N. & Bilhartz, R.D., 2011, p. 696). A plethora of these risk factors contribute to the severity of symptomology as well as dictating the type of pregnancy outcome.

Symptomology and Patient Outcomes

The symptomology of hypertensive disorders of pregnancy (i.e., preeclampsia, gestational hypertension) are variable and dependent upon the severity of clinical manifestations. Mild preeclampsia is diagnosed based on the presence of new onset hypertension and proteinuria. It is confirmed by "after 20 weeks' gestation, a blood pressure of 140 mmHg systolic or 90 mm Hg diastolic on at least two occasions 6 hours apart in a woman previously normotensive before pregnancy" (Davidson, et. al., 2012, p. 464). With mild preeclampsia, a gold standard for measuring proteinuria is conducted using a 24-hour urinalysis, and it is generally found to be between 300 mg/L (1+ dipstick) and 1 g/L (2+ dipstick), adjusted based on creatinine level and urine concentration. Oftentimes, generalized edema of the face, hands, ankles, and lower legs is present, although it is no longer considered a diagnostic criterion. Edema is identified by a weight gain of more than 1.5 kg/month (3.3 lb) in the second trimester or more than 0.5 kg/week (1.1 lb) in the third trimester. In order to diagnose more severe preeclampsia, blood pressure must be 160/110 mm Hg or higher on two occasions at least 6 hours apart while the woman is on bed rest, proteinuria of 5 g/L or higher in 24 hours or 3+ or greater on two random urine samples collected at least 4 hours apart, and significant oliguria (urine output less than or equal to 500 mL in 24 hours). Other clinical manifestations of worsening preeclampsia include severe headache and visual disturbances, dyspnea and cyanosis related to pulmonary edema, epigastric or right upper quadrant pain, nausea and vomiting, impaired liver function, thrombocytopenia, and the development of eclampsia (characterized by the sudden onset of convulsions and seizures, resulting in coma and possibly fatal). The type of patient outcome is determined by the combination of risk factors, the severity of these symptoms, and the effectiveness of treatment. (Davidson, et. al., 2012)

Treatment

Chronic hypertension is treated by promoting frequent rest periods, enforcing sodium limitations (of about 2.4 g per day) and by emphasizing the importance of gaining the recommended amount of weight during pregnancy. Unless blood pressure is found to be greater than 150-160/100-110 mm Hg, antihypertensive medications are not generally indicated for use during pregnancy, yet if it is absolutely essential, Methyldopa or Labetalol are the therapeutic first choice drugs used as treatment. Furthermore, more constant and consistent blood pressure monitoring and fetal surveillance are essential, including but not limited to keeping a record of fetal movement and serial ultrasonography to assess fetal growth & development as well as amniotic fluid volume. "Laboratory work includes a urinalysis and culture; 24-hour urine for protein, creatinine clearance, sodium, and potassium; CBC; serum electrolytes; and a glucose tolerance test" (Davidson, et. al., 2012, p. 476). It has been suggested that the use of low-dose aspirin (50 to 150 mg daily) beginning between 12 and 18 weeks' gestation can be used as a primary prevention among high-risk women in order to reduce the risk of developing preeclampsia. This is because of its known inhibitory effect on prostaglandin production, lowering levels of thromboxane, which would limit vasoconstriction, ultimately lowering blood pressure. In addition, several dietary approaches have been implemented, such as vitamin supplementation with zinc, calcium, magnesium, Vitamin D, fish oil, and antioxidants (Vitamins C and E), yet evidence to support their effectiveness is inconclusive and unclear, so they are not routinely prescribed on a prophylactic basis to prevent preeclampsia. Finally, a woman with chronic hypertension generally has more frequent prenatal visits and should be seen every 2 to 3 weeks in the first two trimesters and then more often in the third trimester, depending on maternal health and fetal stability. "The placenta plays a central role in the development of the

disease, for which the only known cure is birth of the fetus and removal of the placenta" (Davidson, et. al., 2012, p. 461). Therefore, in general, the focus of treatment is management of symptoms and reduction of risk factors (in particular, the problem of obesity and excessive weight gain) that contribute to the pathophysiology and severity of symptoms in preeclampsia.

B. Gestational Diabetes

Definition

"Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy" (Davidson, et. al., 2012, p. 423), in that it is the clinical manifestation of glucose intolerance. It occurs more often along with superimposed preexisting diabetes mellitus, yet is also secondary to the inability of carbohydrate metabolism to properly compensate for the added stress of pregnancy, and is a direct consequence of altered maternal metabolism stemming from changing insulin resistance and rising hormonal levels. These normal physiological changes of pregnancy that increase insulin demands to counteract the effects of accelerated carbohydrate metabolism are compounded by the vascular degeneration that progresses as a result of obesity and excessive weight gain during pregnancy. The early diagnosis of GDM is essential because even in its mildest form, it significantly increases the risk of perinatal morbidity and mortality. (Davidson, et. al., 2012)

Pathophysiology

Carbohydrate metabolism is altered early in pregnancy by a rise in hormone levels, specifically estrogen and progesterone. These hormones stimulate maternal insulin production and increase tissue response to insulin. "The pathophysiology of GDM involves both decreased insulin sensitivity and insufficiency of insulin secretion, resulting in hyperglycemia. Decreased insulin sensitivity causes the limited ability of insulin to transport glucose from the intravascular

into peripheral tissues such as skeletal muscle and adipose, suggesting that obese women are more likely to be at a greater risk for the development of GDM" (Sugiyama, Watanabe, Takimoto, Fukuoka, Yoshiike & Sagawa, 2009, p. 223). Later on in pregnancy, the woman demonstrates prolonged hyperglycemia related to increased glucose use and glycogen storage to meet maternal metabolic needs as well as fetal growth, and begins to exhibit hyperinsulinemia to meet increased insulin requirements. The high levels of circulating insulin causes increased maternal peripheral resistance to insulin because of placental secretions, ensuring high circulating levels of maternal glucose available for diversion to the growing fetus to meet their metabolic needs. The physiologic changes of pregnancy and the pathophysiology of obesity can drastically alter insulin requirements and accelerate the progress of vascular disease secondary to preexisting diabetes. (Davidson, et. al., 2012)

Symptomology and Patient Outcomes

The influence of pregnancy on diabetes is profound, in that the normal physiological changes that occur naturally reinforce the severity of diabetic symptomology. Numerous factors, namely the extreme variability in insulin requirements, make effective control over and management of diabetes throughout pregnancy much more difficult to achieve. As pregnancy progresses, the renal threshold for glucose declines, leading to an increased risk for ketoacidosis. The usual laboratory test for diagnosing pre-gestational diabetes mellitus, glycosylated hemoglobin (HbA1c), has not been found to be reliable for screening of GDM and has therefore not been recommended for diagnostic purposes. GDM is diagnosed when two or more of the following values are met or exceeded: the fasting glucose is $\geq$ 95 mg/dl, $\geq$ 180 mg/dl after 1 hour, $\geq$ 155 mg/dl after 2 hours, or $\geq$ 140 mg/dl after 3 hours. The classic signs and symptoms of diabetes are polyuria (frequent urination), polydipsia (excessive thirst), polyphagia (excessive hunger) and

glycosuria (glucose in the urine). The diabetogenic effect of pregnancy can augment any preexisting disruption in carbohydrate metabolism, and any increased diabetic potential (associated with obesity and excessive weight gain) may precipitate an elevated risk for developing gestational diabetes. In addition, in pregnant women with preexisting diabetes, there is a greater incidence of preeclampsia and eclampsia. (Davidson, et. al., 2012)

Treatment

The treatment for GDM is the same as how regular DM is managed. The primary concern for the pregnant woman with GDM and/or preexisting DM is strict control of circulating blood glucose levels. If control is achieved and maintained, diabetes generally does not worsen during pregnancy. The focus for management should be ensuring appropriate gestational weight gain, normoglycemia, and the absence of ketoacidosis by following proper dietary guidelines, in order to avoid the excessive use of insulin therapy. Overall, there needs to be a concern with maintaining appropriate weight and gaining within recommendations throughout pregnancy in order to best manage the amount of glucose to be at acceptable levels to successfully promote positive outcomes and avoid maternal and fetal complications. (Davidson, et. al. 2012)

C. Cardiovascular Disease and Peripartum Cardiomyopathy

Definition

Obesity and excessive weight gain coupled with the normal cardiac changes and increased cardiovascular demands that occur during pregnancy confers a much higher likelihood of developing cardiovascular complications. In general, "up to 4% of pregnancies may have cardiovascular complications despite no known prior disease" (Mohamad, Bernal, Thatai & Peterson, 2012, Medscape Reference). It is commonly found that serious cardiac decompensation is underdiagnosed in pregnant women because many of the chief presenting

complaints that would be suggestive of certain types of cardiovascular disease are falsely attributed to the normal physiologic changes that occur throughout pregnancy. "Many of the normal symptoms of pregnancy, such as dyspnea on exertion, orthopnea, ankle edema, and palpitations, are also symptoms of cardiac decompensation" (Mohamad, et. al, 2012). In particular, "peripartum cardiomyopathy is a dysfunction of the left ventricle that occurs in the last month of pregnancy or the first 5 months postpartum in a woman with no previous history of heart disease" (Davidson, et. al., 2012, p. 442). With this in mind, it can make it very hard for health professionals to provide an early and quick diagnosis because often the first signs and symptoms of severe heart problems in pregnancy arise at the stage of acute cardiac decompensation. "Gestational diabetes, preeclampsia, preterm birth, and birth of an infant small for gestational age are ranked as major risk factors for CVD" (Mohamad, et. al, 2012). The best way possible to slow down the progression of the pathophysiology of CVD is to eliminate these risk factors and break the cycle of obesity.

Pathophysiology

The exact cause of peripartum cardiomyopathy is unclear although the pathophysiology of its symptoms has been linked to genetic predisposition, as well as the cardiovascular changes that occur secondary to obesity, which are attributed to chronic hypertension and preeclampsia. "Peripartum cardiomyopathy is characterized by its rapid clinical course and a probability for spontaneous recovery" (Bhattacharyya, Basra, Sen & Kar, 2012, p. 8). Even so, controlling or alleviating the risk factors associated with the development of CVD should be the primary focus when dealing with symptoms, providing treatment, and ensuring the best pregnancy outcomes.

Symptomology and Patient Outcomes

The presentation of signs and symptoms of PPCM is very similar to any other type of cardiovascular disease or heart failure. Common symptoms include dyspnea (shortness of breath), orthopnea (SOB with changes in positioning), cough, and hemoptysis. Usually, the patient is designated with a Class III or IV NYHA level of cardiac functioning. Additional symptoms include nonspecific fatigue, malaise, palpitations, chest and abdominal pain/discomfort, and postural hypotension. Common signs of PPCM include displacement of the apical impulse, presence of a S3 heart sound, evidence of mitral or tricuspid regurgitation, jugular venous distention/engorgement, pulmonary crackles, hepatomegaly, and peripheral edema, especially in the feet. The patient usually begins to show signs of anemia and infection, and the treatment revolves around focusing on the underlying abnormality that is precipitating the symptoms of the disease. (Bhattacharyya, et. al., 2012)

Treatment

The treatment and management of PPCM is equally analogous to any other type of cardiovascular disease or heart failure. These include but are not limited to oxygen, diuretics, beta blockers, calcium channel blockers, digoxin, inotropic agents, anti-arrhythmics (to prevent and/or treat atrial fibrillation), and anticoagulants (to prevent thromboembolism).

The prognosis of women who are diagnosed with peripartum cardiomyopathy is most dependent upon how efficiently the heart recovers its functional capacity after childbirth. Luckily, it has been consistently proven that about 50% of patients have substantial improvement in cardiac symptoms and recovery of left ventricular function, and 30% of patients return to baseline function within 6 months after diagnosis. “The prognosis is best when peripartum cardiomyopathy is diagnosed and treated early. Fortunately, despite a mortality rate of up to 10%

and a high risk of relapse in subsequent pregnancies, many patients with peripartum cardiomyopathy recover within 3 to 6 months of disease onset" (Bhattacharyya, et. al., 2012, p. 14). "The usual causes of death in patients with peripartum cardiomyopathy (PPCM) are progressive heart failure, arrhythmia, or thromboembolism. The mortality rate related to embolic events has been reported to be as much as 30%" (Carson & Jacob, 2011, Medscape Reference).

In general, most women are strongly discouraged to have future pregnancies, specifically among those who have persistent left ventricular dysfunction, because of the high risk of recurrence that PPCM carries with it. The main concern lies at the center of why women with unresolved PPCM-related cardiac dysfunction with the fact that these women with weakened hearts will not be able to endure the increased cardiovascular workload that is associated with normal pregnancy. If they do become pregnant again, these women will be at a greater risk of developing worsening cardiovascular disease and heart failure. "The risk of heart failure and death in women with persistently decreased left ventricular function may be as high as 20% with subsequent pregnancy" (Mohamad, et. al., 2012). Regarding those who did have subsequent pregnancies, the literature suggests that a significantly larger percentage of these women had normal outcomes after fully recovering their cardiac function, whereas a dismally lower percentage endured normal pregnancies when plagued with persistent cardiac dysfunction.

"History of hypertension, preeclampsia, and eclampsia are each associated with a higher incidence of peripartum cardiomyopathy, but no causal association has been shown. The existing literature indicates that most patients with peripartum cardiomyopathy have myocardial inflammation" (Bhattacharyya, et. al., 2012, p. 9). It is evident that more research needs to be conducted to determine the nature and extent of the relationship between PPCM, hypertension,

preeclampsia, and how the pro-inflammatory pathophysiology that obesity and excessive weight gain during pregnancy triggers adverse maternal and fetal outcomes.

I. Fetal and Neonatal Complications

A. Fetal Macrosomia (Large for Gestational Age)

Mothers with diabetes usually have infants who are large for gestational age (LGA) as a result of high levels of fetal insulin production stimulated by the high levels of glucose crossing the placenta from the mother. "Excessive maternal weight gain during pregnancy was associated with a doubling of the risk of large for gestational age neonates" (Smith, et. al, 2008, p. 179), which is related to sustained fetal hyperinsulinism and hyperglycemia that lead to excessive growth through fat deposition. Consequently "Overweight women who gain more gestational weight than recommended are two to four times more likely to have a macrosomic infant than those whose gestational weight gain is within IOM guidelines" (Langford, et. al., 2011, p. 861). "Large for gestational age offspring are subsequently at an increased risk of birth trauma, including shoulder dystocia and brachial plexus injury and for developing metabolic syndrome (obesity, insulin resistance, and hyperlipidemia) in childhood, even in the absence of maternal diabetes" (Smith, et. al, 2008, p. 179). In other words, the cycle of obesity is perpetuated within the infants of obese women with diabetic complications.

B. Prematurity and Low Birthweight

Obesity and excessive weight gain in pregnancy has been associated with an increased incidence in prematurity of newborns and consequently an elevation in the number of low birthweight infants. More specifically, "preeclampsia is a primary cause of placental insufficiency and premature birth" (Davidson, et. al., 2012, p. 464), meaning that infants born to preeclamptic mothers tend to be small for gestational age (SGA) related to intrauterine growth

restriction (IUGR) that is specifically associated with maternal vasospasm and hypovolemia, which result in fetal hypoxia and malnutrition throughout pregnancy. During labor & delivery, placental abruption secondary to preeclamptic hypertension is also very likely to occur. "Maternal morbid obesity is also associated with an increased risk of poor fetal growth. Obese women are also at greater risk of delivering a VLBW infant" (Smith, et. al, 2008, p. 179), because infants of mothers with diabetes who have vascular involvement may demonstrate intrauterine growth restriction (IUGR) related to decreased placental perfusion. "Overweight women who either gain less than 0.25 lbs per week (much below recommendations) or more than 1.75 lbs per week (in great excess of recommendations) are at an increased risk for preterm delivery compared to normal weight women who gain within the recommended guidelines" (Langford, et. al., 2011, p. 861). Overall, maternal obesity and excessive weight gain during pregnancy have already been directly linked to gestational hypertension and preeclampsia, so this indirectly leads to higher rates of premature birth and very low birthweight secondary to placental insufficiency and thwarted fetal growth.

C. Cesarean Delivery and Birth Complications

Obesity, pre-pregnancy weight, and excessive weight gain in pregnancy has been associated with an increased risk in cesarean deliveries either as elective procedures or in emergent situations related to significant maternal and/or neonatal complications. More often than not, cesarean deliveries are performed in order to prevent birth complications such as placental abruption or fetal shoulder dystocia during labor, which are secondary to gestational hypertension, preeclampsia, and gestational diabetes. Many conditions that are related to obesity and excessive weight gain during pregnancy also lead to a higher incidence of birth defects. In particular, "the incidence of congenital anomalies in diabetic pregnancies is 5% to 10% and is

the major cause of death for infants of mothers with diabetes" (Davidson, et. al., 2012 p. 424). "In women with known pre-gestational diabetes, abnormal HbA1c values correlate directly with the frequency of spontaneous abortion and fetal congenital anomalies. A value greater than 10% is associated with a fetal anomaly rate of 20% to 25%" (Davidson, et. al., 2012, p. 425). These anomalies most often involve the heart (septal defects, coarctation of the aorta, transposition of the great vessels), the central nervous system (CNS), including hydrocephalus, meningo-myelocele, and anencephaly. Furthermore, respiratory distress syndrome (RDS) can happen more frequently due to the inhibitory effects that high levels of fetal insulin have on the fetal enzymes required for surfactant production in the lungs.

Preventions and Future Strategies

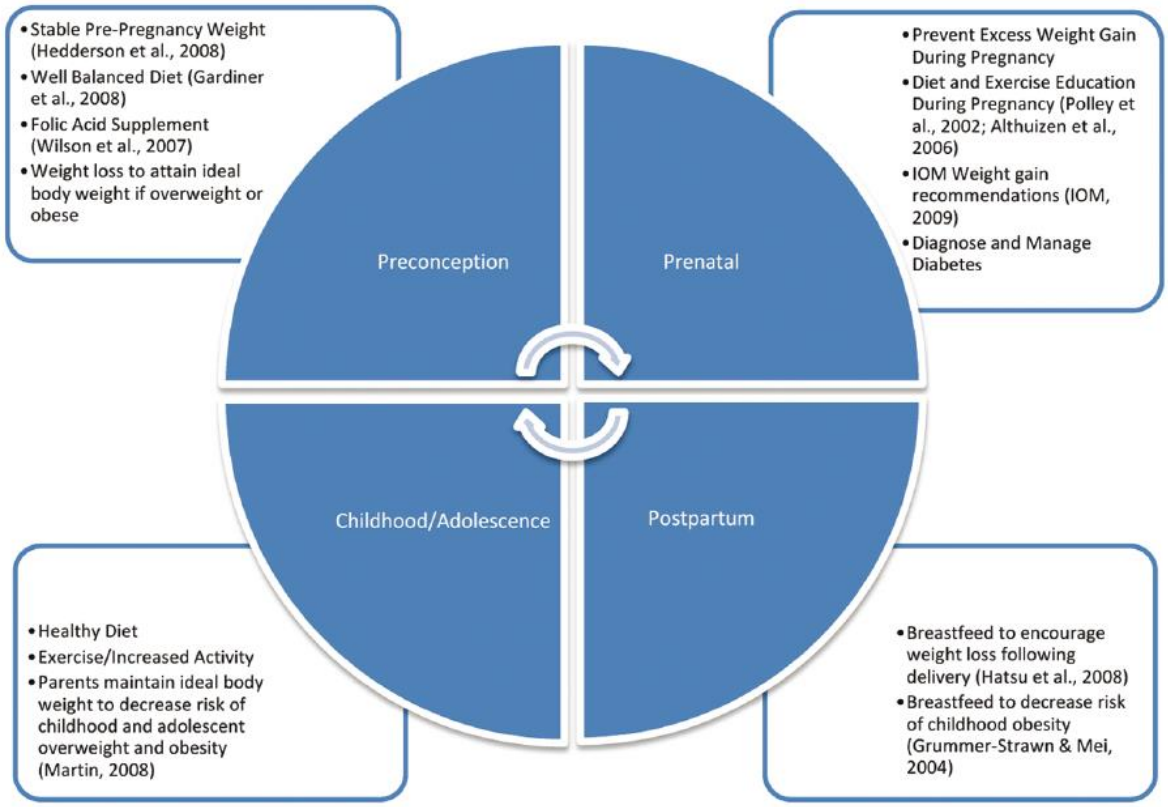


Figure 1: Evidence Based Strategies to Break the Cycle of Obesity

Walters & Taylor, Maternal obesity: consequences & prevention strategies, *Nursing for Women's Health,* 13(6), 2009-2010, p. 493

Overall, there must be more emphasis placed on teaching and education to promote healthy lifestyle choices, including weight loss, maintenance, and control, prior to, throughout, and following pregnancy. In addition, preconception assessment and counseling are strongly encouraged and should include the provision of specific information concerning individualized maternal and fetal risk factors associated with obesity and excessive weight gain in pregnancy. Furthermore, nutrition consultation and exercise counseling should be offered to all overweight or obese women during pregnancy and should be continued postpartum and before attempting another pregnancy. This is essential in order to reduce the likelihood of developing long-term, chronic postpartum complications, such as permanent weight retention and the prolonged elevations in BMI that follow it. "During pregnancy, individual weight management plans need to be developed stressing calorie composition and the need for increased protein consumption in the first trimester. This content can also be included in prenatal education programs, especially early pregnancy classes. Last, concerns of excessive pregnant weight gain contributing to postpartum weight retention leading to a risk developing diabetes and hypertension need to be stressed" (Smith, et. al., 2008, p. 181). "The IOM guidelines for maternal weight gain in pregnancy provide an estimate for population goals but may be inadequate for individual patient needs. Other factors such as resting metabolic rate and the degree of maternal insulin resistance, especially in obese women, and the quantity and type of exercise may be more predictive of actual nutritional requirements during pregnancy" (Smith, et. al., 2008, p. 177). "Past research on maternal weight gain during pregnancy has focused on determinants and consequences of inadequate weight gain with concerns for the health of the infant. However, with the rising prevalence of obesity among women of childbearing ages and the high proportion of women who are gaining in excess of recommendations during pregnancy, a shift in research focus must

include consideration on the mother's long term health status" (Smith, et. al., 2008, p. 182). All in all, the evidence-based practices of nutrition and exercise education and regimen adherence, the management of preexisting conditions prior to pregnancy, gaining appropriate gestational weight within the recommendations during pregnancy, and weight loss or maintenance prior to, throughout, and following pregnancy (facilitated by breastfeeding) should be implemented to break the cycle of obesity to allow for improved maternal and fetal pregnancy outcomes.

Conclusion

To conclude, the relationships between maternal obesity class, gestational weight gain, and maternal and newborn outcomes are complex. The pathophysiology of obesity along with the normal physiological changes of pregnancy mutually contributes to several adverse maternal and neonatal/fetal outcomes. It is important to emphasize the need for preconception assessment and counseling about reducing risk factors specific to obesity and exercising weight control by following weight gain recommendations throughout pregnancy. Overall, there is a lack of consistency in focus on how to prevent the negative maternal and neonatal/fetal outcomes associated with obesity and excessive weight gain. This is a gap in research that must be further addressed and discussed among health professionals in order to promote healthy pregnancy outcomes and to ensure long-term maternal and fetal health.

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